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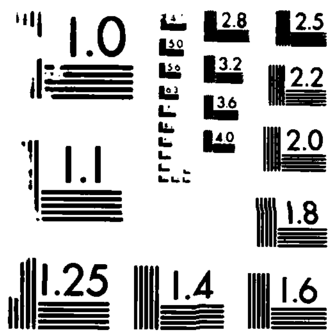
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Human Cerebral Function at High Altitude

Final Report

Brenda D. Townes, Ph.D.
Thomas F. Hornbein, M.D.
Robert B. Schoene, M.D.

March 1985

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U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
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University of Washington
Seattle, Washington 98195

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Between 1981 and 1984, mountaineers from five separate expeditions to Mount Everest were given a series of two neurological exams, the first immediately prior to their climb and the second shortly after their return. These expeditions afforded an opportunity to study the consequences of extreme sustained hypoxia on human cerebral function. The goal was to ascertain whether exposure of healthy acclimatized individuals to extreme high altitude results in subsequent long-term alterations in cognition and behavior

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Subjects were 51 members of ~~five~~ expeditions to Everest between the years 1981 to 1984. All but five subjects were males; with ages from 24 to 54 years; with an average of 18.1 years of education. The neuropsychological exams were administered to subjects at approximately three weeks before arrival at base camp and again at approximately two to three weeks after completion of the climb.

In this young and highly educated group of subjects using supplemental oxygen to climb Mount Everest, some neurobehavioral effects were found after exposure to the hypoxia of extreme altitude. A mild deterioration in expression of verbal material was observed. A bilateral reduction in motor speed characterized by rapid muscle fatigue was also evident. One hypothesis is that cerebellar and/or motor cortex functions are negatively affected by prolonged exposure to hypoxia at altitude. There also appears to be some involvement of the temporal lobe, as indicated by the reduction in verbal ability.

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SUMMARY

Between 1981 and 1984, mountaineers from five separate expeditions to Mount Everest were given a series of two neuropsychological exams, the first immediately prior to their climb and the second shortly after their return. These expeditions afforded an opportunity to study the consequences of extreme sustained hypoxia on human cerebral function. The goal was to ascertain whether exposure of healthy acclimatized individuals to extreme high altitude results in subsequent long-term alterations in cognition and behavior indicative of hypoxic brain dysfunction.

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In this young and highly educated group of subjects using supplemental oxygen to climb Mount Everest, some neurobehavioral effects were found after exposure to the hypoxia of extreme altitude. A mild deterioration in expression of verbal material was observed. A bilateral reduction in motor speed characterized by rapid muscle fatique was also evident. One hypothesis is that cerebellar and/or motor cortex functions are negatively affected by prolonged exposure to hypoxia at altitude. There also appears to be some involvement of the temporal lobe, as indicated by the reduction in verbal ability.

FOREWORD

For the protection of human subjects, the investigator(s) have adhered to policies of applicable Federal Law 45CFR46.

HUMAN CEREBRAL FUNCTION AT HIGH ALTITUDE

Between 1981 and 1984, mountaineers from five separate expeditons to Mount Everest completed a series of pre- and post-expedition neuropsychological exams. These expeditions afforded an opportunity to observe the consequences of extreme sustained hypoxia on human cerebral function. Our goal was to ascertain whether exposure of healthy acclimatized individuals to extreme high altitude results in subsequent long-term alterations in cognition or behavior indicative of hypoxic brain dysfunction.

Laboratory studies of the effect of acute hypoxia upon cognition have been carried under simulated conditions. These investigations suggest impaired sensory perceptual and motor performance at altitudes to 6100 m (3,7,9). While mild hypoxia (to 2,314 m) may improve performance on simple motor tasks, more time is required to learn a new task at 3,048 m. The mountaineer, therefore, might perform routine, well-practiced tasks adequately but be impaired in performing under unpracticed emergency conditions (5).

Naturalistic observations of alpine mountaineers suggest an increasing impairment in sensory, motor, and complex cognitive abilities as a function of severity of hypoxia with increasing altitude. At the highest altitudes the mountaineers' behavior may be similar to an individual with a known acute organic brain syndrome (10).

How do increasing degrees of oxygen deprivation, possibly along with extreme climatic conditions, produce the observed cognitive and behavioral changes? Selvamurthy, Saxena, Krishnamurthy, Suri, and Malhotra (14) made electroencephalographic recordings of 10 high altitude native and 10 lowlander soldiers at sea level and at 3,500 m. Compared to native highlanders, lowlanders showed an increase in alpha activity during acclimatization suggestive of cortical depression. This change was associated with lethargic behavior attributed to cerebral hypoxia. Forster, Soto, Dempsey, and Hosko (6) recorded the electroencephalographic and visual evoked responses of seven healthy male subjects at sea level and for 12 successive days at altitude 4,300 m. No changes in cerebral electrical activity were noted in the first two to three hours of hypoxia. Two subjects showed electrical changes during the first four days suggesting cortical depression. All remaining subjects showed electrical changes after the fifth day indicative of cortical excitation. Simultaneous changes in behavior were noted including anorexia, insomnia, irritability, increased ventilation, and depression. These data suggest that cognitive and behavioral changes observed during hypoxia at high altitudes were associated with measurable alterations in central nervous system function. In addition, individual differences during the initial stages of acclimatization occur in both the type and rate of change in cerebral electrical activity.

The physiological, cognitive and behavioral changes occurring at high altitudes are presumed to be caused by alteration in oxygenation of the tissues. In acute hypoxia a reduction of arterial blood saturation to 85% leads to a decreased capacity for mental concentration and abolishes fine muscular coordination. A reduction to 75% leads to faulty judgment, emotional lability and impairment of muscular function (1).

The permanence of cognitive and behavioral changes observed at high altitudes once the hypoxic episode is resolved was investigated by Clark, Heaton and Wiens (4). They tested 22 mountaineers prior to and 16 to 221 days following Himalayan climbs above 5,100 m on an extensive battery of psychological and neuropsychological measures (*Wechsler Adult Intelligence Scale, Halstead Reitan Neuropsychological Test Battery*, etc.). They found no evidence of permanent cerebral dysfunction due to altitude exposure. Sharma, Malhotra, and Baskaran (15,16), by contrast, found that lowlanders required to live for 10 months at high altitudes initially experience impairment of both motor coordination and speed; while the former resolved within a year, the latter persisted over a two year period. Ryn (13) followed a group of 20 male and 10 female Polish alpinists during and "for several weeks" after a Himalayan expedition. Only the male climbers ascended over 5,500 m. Of these, half experienced symptoms similar to an acute organic brain syndrome; "for several weeks after the expedition they continued to feel poorly, showing signs of apathy and abulia, and impaired memory" (p. 461). In addition, 11 out of the 30 climbers (6 men and 5 women) had an abnormal EEG during the immediate period following the climb. On psychological testing (Bender and Graham Kendall) visual motor performance was normal in only 13, borderline in 12, and suggestive of organic pathology in 5 climbers. Although no pre-ascent measures were reported, these data tentatively suggest individual differences in the degree to which cognitive, behavioral, and central nervous system disturbances persist following a prolonged hypoxic episode.

Townes, Hornbein, Schoene, Sarnquist and Grant (17) administered neuropsychological tests to 21 members of the 1981 American Medical Research Expedition to Mt. Everest. Tests were given prior to the expedition, during the ascent, immediately following descent, and at one year post-expedition. Results showed mild deterioration in learning, memory, and expression of verbal material to be present within three days of descent but were resolved by one year later. A bilateral reduction in motor speed characterized by rapid muscle fatigue persisted one year after the expedition. The present study was an attempt to replicate these findings using data collected from five separate expeditions.

METHODS

Subjects:

Subjects were 51 members of the following expeditions: American Medical Research Expedition to Everest (1981), American China Expedition (1982), Mayama Tirich Mir Expedition (1982), Men and Women on Everest (1983), and the American Ultima Thule Expedition (1984). All but five of the subjects were male and ages ranged from 25 to 52 years, with a mean age of 34.9. Twenty-four subjects had M.D.s or Ph.D.s, with an additional 12 having post-graduate education. The mean number of years of education was 18.1. The average altitude attained was 24,000 ft.

Procedures:

Prior to the expedition, a group of neuropsychological tests were administered to subjects at neuropsychological labs at one of the following facilities: University of Washington, San Diego Veterans Administration

Medical Center, or the San Francisco Veterans Administration Medical Center. The test battery included the *Aphasia Screening Test*, *Trail Making B*, *Finger Tapping* and, in some cases *Category and the Tactual Performance Test* from the *Halstead Reitan Neuropsychological Test Battery* (11); *Digit Vigilance*, *Digit Symbol*, and *Visual Search* from the *Repeatable Cognitive-Perceptual-Motor Battery* (8); the *Logical* (verbal) and *Visual* portions of the *Wechsler Memory Scale* (12), and the *Selective Reminding Test* (2).

Subjects were tested just prior to departure and again at approximately two to three weeks after their descent. Data were analyzed by means of the *Wilcoxon Signed Rank Test* to compare differences in performance for those subjects completing both pre- and post-expedition test batteries (n=44).

RESULTS

Table 1 summarizes the significant changes found between pre-expedition, post-expedition, and follow-up performance on the neuropsychological tests. Of 27 comparisons nine were statistically significant. Performance improved between the pre- and post-testing periods on measures of complex problem-solving including spatial problem-solving (*Tactual Performance Test*) and abstract reasoning (*Category*). This improvement is attributed to practice effects. However, the number of errors on *Category* increased with the maximum altitude attained ($\underline{r} = 0.44$, $p < 0.01$). The time required to do the *Tactual Performance Test* with both hands also increased as the altitude attained increased ($\underline{r} = 0.42$, $p < 0.05$) (see Table 1, page 7).

The previous finding of decline in memory and verbal learning (19) was not replicated. Heaton's modification of the *Logical* (verbal) and *Visual* performance were not significant. The decrease in delayed visual recall was found to be significant among those climbers who had reached altitudes of 18,000 ft. or more ($z = 2.01$, $p < 0.05$).

On the aphasia *Screening Test* there was a significant increase in the number of expressive language errors made between pre- and post-expedition ($z = 2.07$, $p < 0.05$). The types of errors made are shown in Table 2. In areas other than arithmetic, these errors were very rare prior to the ascent and, furthermore, are not expected among such young, healthy, and intelligent subjects. Pearson product moment correlations were computed between highest altitude attained and change in pre- and post-expedition performance. Altitude attained significantly correlated with an increase in the number of aphasia errors ($\underline{r} = 0.29$, $p < 0.05$). There was no significant increase in construction dyspraxia (see Table 2, page 8).

Finger Tapping speed showed a significant decrease at the post-expedition testing for both right hand ($z = 3.37$, $p < 0.001$) and left hand ($z = 2.11$, $p < 0.05$). The standard method of administering the *Finger Test* is to obtain five trials of ten seconds each on each hand. To reach criterion for the test, the difference between trials should not exceed five taps. Ability to maintain motor speed to criterion dropped significantly between the pre- and post-tests ($z = 2.67$, $p < 0.01$).

Table 1. Wilcoxin Signed Rank Tests Comparing Pre- and Post-Expedition Performance

Direction of Change	Variable	Time	$\bar{X}$	SD	Pre-Post Z	(N)	Above 18 K Z	(N)
A. Improved Performance								
	Tactual Performance Tests							
	Right Hand	Pre-	4.95	1.83	3.50***	(28)	3.568***	(27)
		Post-	3.94	1.35				
	Memory	Pre-	8.60	1.16	2.42*	(28)	2.31*	(27)
		Post-	9.12	.80				
	Localization	Pre-	4.93	2.66	2.52*	(28)	2.31*	(27)
		Post-	6.10	2.61				
	Category (Errors)	Pre-	27.57	21.18	4.49***	(28)	4.40***	(27)
		Post-	21.41	46.75				
	Digit Vigilance (Omits)	Pre-	3.41	3.07	1.87	(36)	2.06*	(30)
		Post-	2.55	3.34				
B. Decline in Performance								
	Finger Tapping							
	Right Hand	Pre-	54.06	4.88	3.37***	(39)	3.44***	(33)
		Post-	50.05	7.35				
	Left Hand	Pre-	49.04	5.92	2.11*	(39)	2.89*	(33)
		Post-	45.84	6.84				
	Criterion	Pre-	.85	.37	2.67**	(19)	2.67**	(18)
		Post-	.46	.51				
	Aphasia Verbal Errors	Pre-	.85	.37	2.67**	(19)	2.67**	(18)
		Post-	1.05	1.12				
	Wechsler Memory Scale							
	Long-Term Visual Recall	Pre-	11.83	2.43	1.62	(39)	2.01*	(33)
		Post-	11.12	2.11				

* $p < 0.05$
** $p < 0.01$
*** $p < 0.001$

Table 2. Types of Aphasia Errors at Post Test

Type of Error	Item	Response
1. Reading	7 SIX 2	6 - 7 - 6 - 2
	He is a friendly animal, a famous winner of dog shows	He is a friendly animal, a famous winner of show d... dog shows
2. Writing	SQUARE	Ssquare, Squore
	warning	warninG, waring, narning
3. Calculation	85 - 27 =	52, 55, 68
	17 x 3 =	49, 52, 57, 41
4. Spelling	triangle	trangle, tringle
5. Pronunciation	Massachusetts	Massachusess, Massachutetts, Massatushetts
	Episcopal	Ekpiscopal, Episcabal
6. Confusion of Body Parts	Place left hand to right ear	Right hand placed to right ear, Left hand placed to right eye
	Place left hand to left elbow	Right hand placed to left elbow
7. Explanation	He shouted the warning	"He wanted to tell everyone the house was on fire." (Concrete response)
8. Naming	Cross	red cross
	Clock	Eleven o'clock
9. Repeating	He shouted the warning	He shouted out a warning

DISCUSSION

In this young and highly educated group of subjects using supplemental oxygen to climb Mount Everest, residual neurobehavioral effects were found after exposure to the extreme hypoxia of high altitude. These impairments were evident at testing sessions averaging 23 days after return from base camp.

Ryn (13) and Townes, Hornbein, Schoene, Sarnquist and Grant (17) found signs of memory impairment on post-expedition tests. Townes' findings showed memory impairments present within three days of descent into Kathmandu but not one year later. Although the only statistically significant memory problem supported by this study was in delayed visual recall among climbers who had reached altitudes above 18,000 ft., these climbers frequently reported noticeable memory problems while at high altitudes. It appears that any such deficits were quickly resolved and were not longer present at this more delayed post-expedition testing session.

The findings of this study support Townes' earlier observation of decrements in verbal expression. Such findings suggest possible involvement of the temporal area of the brain. Based on previous studies, these expressive verbal difficulties are expected to be transient, and pre-expedition functioning regained within one year post-climb.

This study also supported Townes' findings of bilateral reduction in motor speed characterized by rapid muscle fatigue. As prolonged motor impairments have also been found by Sharma, Malhotra, and Baskaran (15,16), the findings appear to be reliable. This would indicate that motor cortex functions may be negatively affected by prolonged exposure to hypoxia at high altitude. There may also be some involvement of cerebellar functions. These hypotheses may be tested in the future by using a test battery designed to further distinguish between motor speed and coordination.

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